

REMARKS

Applicants respectfully request reconsideration of the present case in view of the above amendments and the following remarks.

Claims 1 and 12 have been amended. Claim 1 has been amended to clarify the invention and is supported throughout the specification including at page 17, line 10 to page 18, line 13. Claim 12 has been amended to be consistent with the amendment to claim 1.

Applicants also submit that the claims as amended do not require additional search or further consideration. Applicants have elected, for search purposes, an amine moiety as a nucleophile, and that the released proteins are analyzed by mass spectroscopy. Nucleophiles such as amine groups, were searched by the examiner and were originally claimed in claim 7. Any search of B elimination of glycosylation sites as required in claim 1 would include O-glycosylation sites as evidenced by the citation of Wells et al. A search of analysis of proteins by mass spectroscopy would include analysis of proteins having a molecular weight of 5000 daltons or less.

Claims 7, 24-26 have been cancelled without prejudice or disclaimer. Claims 24-26 have been cancelled due to a restriction requirement. Applicants reserve the right to file a divisional application concerning the subject matter of these claims. Applicants reserve the right to file a continuation application concerning the subject matter of claim 7.

Interview Summary

Applicants thank the Examiner for the interviews conducted on January 21, and January 23, 2008. We discussed allowability of the claims. Applicants are submitting this amendment in response to the interview.

Clarification Request

Applicants request clarification of the statements of the examiner regarding the election of species. Applicants request that the examiner confirm that if claim 1 is found allowable, then the examiner must consider claims to additional species written in dependent form or claims that otherwise include all of the limitations of the generic claim

Rejection under § 112, first paragraph

The Examiner rejected claims 1–23 under § 112, first paragraph, for lack of written description. Specifically, the Examiner contends that the specification does not provide written description for the full breadth of glycosylated proteins and nucleophiles. Applicants respectfully traverse this rejection.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed. Reg. 1099, 1105 (2001); *see also*, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Applicants claim 1 is now directed to "A method for separating a deglycosylated protein comprising: obtaining a mixture comprising a glycosylated protein and unglycosylated proteins, wherein the glycosylated protein comprises a protein having an O linked glycosylation site and a glycosyl group bound to the protein via the glycosylation site and has a molecular weight of 5000 daltons or less, contacting the mixture with a resin, wherein the resin comprises a nucleophile bound to a solid support via a linker, wherein said nucleophile is selected from the group consisting of amine, hydroxyl, sulfhydryl, and combinations thereof, said contacting done under conditions sufficient to remove the glycosyl group by β -elimination from the glycosylated protein to yield the deglycosylated protein having an unsaturated intermediate at the deglycosylation site, the deglycosylated protein bound to the solid support via the unsaturated intermediate at the deglycosylation site; rinsing the bound deglycosylated protein, thereby removing unglycosylated proteins; releasing the deglycosylated protein from the solid support."

Applicants submit that one of ordinary skill in the art would understand that Applicants were in possession of the invention as claimed. Applicants submit the claims are directed to

methods and not the glycoproteins or nucleophiles per se. The written description analysis then should focus on the method steps rather than the glycoproteins or nucleophiles themselves, and should be considered in the context of the knowledge in the art. Applicants further submit that the examples are not necessary to support the adequacy of written description, written description can be met where actual reduction to practice is absent; and there is no per se rule that an adequate written description that involves a biological macromolecule must contain a recitation of known structure. *Falko-Gunter Falkner vs. Inglis*, 448 F.3d 1357 (Fed. Cir. 2006). In addition, the description should be evaluated with the scientific and technologic knowledge at the time of filing. Id at 1363.

While not acquiescing to the rejection and solely to expedite prosecution, claim 1 has been amended to refer to a “glycoprotein comprising a protein having an O linked glycosylation site”. The specification describes O linked glycoproteins at page 17, lines 20-31. Applicants submit that one of skill in the art reading the specification as filed would understand that the specification describes the methods as claimed. With regard to the type of glycoproteins, the types of linkages in glycosylated proteins have been characterized and are known to those of skill in the art. As described in the specification, the B elimination reaction is, in the least, applicable to O linked glycoproteins.

The Examiner points to Wells et al. for the proposition that the invention is not enabled because Wells et al. indicates that “some of the O-GlcNAc-modified residues are more resistant to β -elimination.” Applicants respectfully submit that the Wells et al. reference must be read as a whole. Wells et al. teaches that only mild β -elimination conditions were used so as to distinguish O-linked glycosylation sites from that of phosphorylated sites. Under such conditions, certain O-linked glycosylation sites were not readily subject to β -elimination. However, Applicants teach that phosphorylated sites can be removed through use of techniques known to those of skill in the art so that such mild β -elimination conditions taught by Wells et al. may not be required. Applicants also claim such a method in claim 3.

The examiner has the burden to provide evidence why one of skill in the art would not recognize in an applicant’s disclosure a description of the methods defined by the claims. The examiner has cited only one paper that that raises any issue about what one of skill in the art

would understand. Applicants have refuted the statements in this paper by reference to the teachings of the specification.

Applicants have provided structure and function in the claimed methods. Applicants have claimed a method including contacting a mixture comprising a glycosylated protein with a resin, wherein the resin comprises a nucleophile bound to a solid support via a linker, wherein said a nucleophile is selected from the group consisting of amine, hydroxyl, sulfhydryl, and combinations thereof, said contacting done under conditions sufficient to remove the glycosyl group by β -elimination from the glycosylated protein to yield a deglycosylated protein having an unsaturated intermediate at the deglycosylation site, the deglycosylated protein bound to the solid support via the unsaturated intermediate at the deglycosylation site. See also the reaction scheme provided at page 12 in the specification. The claims include both a structural and a functional characterization when considered in the context of the specification and what is known in the art. The structures of nucleophiles are known, and the structures of glycosidic linkages on glycoproteins are known. Thus, applicants submit that one of skill in the art reading the specification would understand that applicants were in possession of the claimed methods.

While not acquiescing to the rejection and solely to expedite prosecution, Applicants' claim 1 now refers to glycoproteins having a molecular weight of 5000 daltons or less and to nucleophiles selected from the group consisting of amine, hydroxyl, sulfhydryl, and combinations thereof. Applicants submit that these amendments address the examiner's written description rejection regarding the genus of glycoproteins and nucleophiles used in the claimed methods.

For the reasons indicated above, Applicants believe that the methods as claimed are enabled, and respectfully request withdrawal of the rejection.

SUMMARY

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
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